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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
12/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/659,295	SCHAEBITZ ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,18,19,105-108 and 114-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 9, 18, 19, 105-108 and 114-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 October 2009 has been entered.

Formal Matters

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Christina Borgeest, Art Unit 1649.

Status of the Claims

Claims 1, 19, 105, 107 and 108 have been amended. Claims 114-117 are new. It is noted that the sequence identifiers of G-CSF have been changed from SEQ ID NO: 28 to SEQ ID NOs: 37, 38 and 39. No explanation is given as to the purpose of this change. Claims 5-7, 12 and 14 are newly cancelled. Claims 1, 9, 18, 19, 105-108 and 114-117 are under examination.

Rejections withdrawn

Claim Rejections - 35 USC § 112, first paragraph – Written Description

The rejection of claims 1, 5-7, 9, 12, 14, 18, 19 and 105-108 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as set forth in previous Office actions is withdrawn in response to Applicants' remarks at p. 5 (whole page) and the first paragraph of p. 6 and in response to the cancellation of claims 5-7, 12 and 14.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 9 and 19 under 35 U.S.C. 102(b) as being anticipated by Whalen et al., (Crit Care Med, 2000; 28: 3710-3717—of record) as set forth in the Office action mailed 16 July 2009 is withdrawn upon reconsideration of the art. Specifically, Whalen examines various neurological parameters (such as BBB damage, brain edema, or brain neutrophil accumulation) after traumatic brain injury (TBI) with a prior administration of G-CSF and finds an increase in damage to the BBB. As Applicants note at p. 7 of their remarks, since Whalen found that all parameters observed after TBI are either unchanged or worsened (BBB damage), the teachings of Whalen as a whole do not support the successful treatment of traumatic brain injury with G-CSF.

Claim Rejections - 35 USC § 103

The rejection of claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. applied to claims 1, 9 and 19 above, and further in view of Brines et al. (2000—of record) as set forth in the Office action mailed 16 July 2009 is withdrawn in response to Applicants' cancellation of claims 5-7.

The rejection of claim 12 under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Deleuze (2000—of record) as set forth in the Office action mailed 16 July 2009 is withdrawn in response to Applicants' cancellation of claim 12.

The rejection of claim 14 under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Morita-Fujimura (1999—of record) as set forth in the Office action mailed 16 July 2009 is withdrawn in response to Applicants' cancellation of claim 14.

The rejection of claims 105-108 under 35 U.S.C. 103(a) as being unpatentable over Whalen et al. as applied to claims 1, 9 and 19 above, and further in view of Neupogen® (Filgrastim) Amgen product information sheet dated 1998—of record as set forth in the Office action mailed 16 July 2009 is withdrawn upon reconsideration of the art. As noted above, Whalen examines various neurological parameters (such as BBB damage, brain edema, or brain neutrophil accumulation) after traumatic brain injury

(TBI) with a prior administration of G-CSF and finds an increase in damage to the BBB, thus the primary reference does not support a protective role of G-CSF in TBI.

New Rejection/Objections

Specification

The disclosure is objected to because of the following informalities: The Brief Description of Drawings does not contain a description of all of the drawings, for instance, there is no description of Figure 2B.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph – Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9, 18, 19, 105-108 and 114-117 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(i) The nature of the invention is complex, as evidenced by the art, which does not suggest that G-CSF can be used to treat TBI. Most recently, Sakowitz et al. (Acta neurochirurgica. Supplement, 2006; 96: 139-43—abstract only, article to follow) teach that 30 minutes following controlled cortical impact injury in rats (a model for TBI), animals were administered G-CSF, however, G-CSF failed to exert protective effects (see abstract). As noted above, Whalen et al. (2000—of record) teach at p. 3712, Figure 1B that G-CSF increases BBB damage. In their conclusions, Whalen et al. do not provide strong support for the protective effect of G-CSF in TBI, but rather point to the unpredictability in the art. For instance, at p. 3716, left column, 2nd paragraph, Whalen et al. state that "functional outcome has not been assessed in this or any other study involving G-CSF administration in the setting of severe [TBI]." They also note in the abstract that further studies are needed in order to evaluate the effects of G-CSF administration on functional outcome in TBI. In a separate article Whalen et al. (Crit Care Med. 1999, 27: 1014-1018—HTML version only available; downloaded 21 December 2009; 9 pages total) reviewed the high degree of unpredictability with regard to whether G-CSF has any protective effect in TBI. Notably, they state that the role of

neutrophils and the acute inflammatory response in the pathogenesis of TBI is an area of controversy (see the bottom of p. 2, last paragraph).

(ii) Given the unpredictability in the art with regard to the role of G-CSF in TBI, one skilled in the art must turn to the specification. There is no guidance in the specification with regard to treatment of TBI with G-CSF. Example 4 addresses amyotrophic lateral sclerosis; Example 5 addresses Parkinson's; Examples 6, 10 and 11 address photothrombotic ischemia; Examples 8 and 12 address neuronal primary culture; Examples 9 and 13 address neural stem cell culture; Example 14 addresses serum half life; Example 15 and 17 address PC12 cell neuroprotection (in vitro); Example 15 addresses that G-CSF is expressed in vivo and Example 18 addresses thromboembolic ischemia. Although the lack of guidance in the specification is alone not sufficient grounds for a rejection under lack of enablement, however, when weighed in conjunction with the art, which fails to show a protective role of G-CSF in treatment of TBI, the preponderance of evidence does not support that G-CSF is effective in the treatment of TBI.

Due to the large quantity of empirical experimentation necessary to determine if G-CSF has a protective role in TBI, the lack of direction/guidance presented in the specification regarding and the absence of working examples directed to the same, the complex nature of the invention, as evidenced by the state of the art, which fails to establish a nexus between G-CSF administration and treatment of TBI, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest

/Bridget E Bunner/
Primary Examiner, Art Unit 1647